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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,541	04/26/2002	Larry A. Wheeler	17400(BAR)	1687

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
10/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/020,541	WHEELER ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,18-22,30,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,18-22,30,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Prosecution on the merits of this application is reopened on claims 16, 18-22, 30, 39 and 40 considered unpatentable for the reasons indicated below:

It is noted that the effective filing date is April 26, 2002, as indicated in the petition decision mailed on August 14, 2002.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 16, 18-22, 39 and 40 rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,465,464 B2 (Wheeler et al.).

The applied reference has a common inventor with the instant application (Wheeler). Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived

from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Wheeler et al. discloses and claims a method of providing neural protection including glaucomatous optic neuropathy to a mammal comprising administering to the mammal suffering from or at risk of suffering a noxious action on its nerve cells an effective amount of brimonidine to inhibit or prevent nerve cell injury or death (claim 1, column 17); wherein the noxious action is a laser light directed into the eye in a procedure for treatment of wet age-related macular degeneration (ARMD) (claim 7, column 18); administering an amount sufficient to achieve a serum concentration of from 0.01 nM to 500 nM (claim 15, column 18) or the compound is administered topically (claim 16, column 18). See also, claim 5.

Laser light directed noxious action for treatment of wet ARMD is disclosed in the specification as the photodynamic therapy (PDT) treatment of wet (neovascular) ARMD, wherein a photosensitive dye is given systemically to a patient, which is taken up only in abnormal tissues such as the abnormal vessels present in wet ARMD. A "cold" laser is directed into the eye, which activates the dye taken up in the cell walls of the abnormal vessels, thus forming oxidative compounds that lead to clot formation in the neovascular tissues. Since the laser treatment can cause photic damage to the retina, the compounds are to be administered to protect the retina from damage by the laser light used as a part of this ARMD therapy. Column 5, line 63-column 6, line 13. The method of administering the compound to the mammal is either systemically, topically, intrathecally, epidurally or by intrabulbuar injection of an effective amount of the aryl-imino-2-imidazolidines including brimonidine. Column 6, lines 30-38. More

preferably, the compounds are administered directly into the eye, either topically or through injection into the eye. Column 7, lines 10-15.

For acute neuroprotective effect such as photoprotection in the laser treatment for ARMD, the protective agent would be administered in advance of the treatment to provide optimal protection during the laser procedure. Column 7, lines 62-66.

Figure 5 exemplifies brimonidine in topical neuroprotection in a dose dependent manner. Column 9, line 55-65, and Figure 5.

The neuroprotective agent should be administered in a dose to achieve a serum or intravitreal concentration of 0.01 nM to 500 mM. Preferably the neuroprotective agent is administered prior to injury to the nerve, but can be administered after injury has occurred to lessen the effect. Column 12, lines 34-53.

4. Claims 16, 18-22, 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,194,415 (Wheeler et al.).

Claim 1 of '415 is drawn to a method of protecting the optic nerve and retina of a mammal comprising administering to the mammal suffering from or at risk of suffering a noxious action on the nerve cells an effective amount of a compound of formula I to inhibit or prevent nerve cell injury or death, wherein the formula encompass brimonidine, and wherein the noxious action includes laser light directed into the eye in a procedure for treatment of wet ARMD. Claim 4 depends from claim 1 and recites that the noxious action is laser light directed into the eye in a procedure for treatment of wet ARMD.

The supporting disclosure to understand the treatment of wet ARMD in the '415 patent claims is the same as for the claims of US 6,465,464 set forth above, since the application that issued as '415 is the continuation parent of the application that issued as '464. However, claims 1 and 4 of '415 recite the method using a generic compound of formula I that encompass brimonidine. Furthermore, Figure 5 exemplifies brimonidine in topical neuroprotection in a dose dependent manner. Column 9, line 55-65, and Figure 5.

5. Claims 16, 18-22, 39 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,248,741 B1 (Wheeler et al.). It is noted that the '741 patent also applies as prior art under 35 USCD 102(a). Therefore, claims 16, 18-22, 39 and 40 are also rejected under 35 U.S.C. 102(a) as being anticipated by U.S. Patent No. 6,248,741 B1 (Wheeler et al.).

The applied reference has a common inventor with the instant application (Wheeler). Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The disclosure of the '741 patent appears to be the same as that of the '415 and '464 patents. It is noted that the claims of the '741 patent are very similar, but narrower in scope than the claims of the '415 patent. Claim 1 of '741 is drawn to a method of protecting the optic nerve

and retina of a mammal comprising administering to the mammal suffering from or at risk of suffering a noxious action on the nerve cells an effective amount of a compound of formula I to inhibit or prevent nerve cell injury or death, wherein the formula encompass brimonidine, and wherein the noxious action includes laser light directed into the eye in a procedure for treatment of wet ARMD. Claim 7 depends from claim 1 and recites that the noxious action is laser light directed into the eye in a procedure for treatment of wet ARMD. Furthermore, Figure 5 exemplifies brimonidine in topical neuroprotection in a dose dependent manner. Column 9, line 55-65, and Figure 5.

Claim Rejections - 35 USC § 103

6. Claims 16, 18-22 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over by U.S. Patent No. 6,465,464 B2 (Wheeler et al.) as applied to claims 16, 18-22 above, and further in view of U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.; previously of record).

The '464 patent teaches a method of using brimonidine in combination with PDT, as indicated above.

The '464 patent does not teach that the method also comprises a therapeutically effective amount of an antiangiogenic compound.

However, Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound (e.g., see abstract; paragraph 18;

claims 20-31, etc.). It is noted that the instant specification acknowledges it was previously known that PDT can result in optic nerve atrophy (See p. 3, first paragraph). It is noted that the effective filing date of the Miller reference, with respect to PDT in combination with an anti-angiogenic agent is 2/10/2000.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wheeler and Miller to create the claimed method with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Miller who teaches using an antiangiogenic compound in combination with PDT.

7. Claims 16, 18-22 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over by U.S. Patent No. 6,194,415 (Wheeler et al.) as applied to claims 16, 18-22 above, and further in view of U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.; previously of record).

The '415 patent teaches a method of using brimonidine in combination with PDT, as indicated above.

The '415 patent does not teach that the method also comprises a therapeutically effective amount of an antiangiogenic compound.

However, Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound (e.g., see abstract; paragraph 18;

claims 20-31, etc.). It is noted that the instant specification acknowledges it was previously known that PDT can result in optic nerve atrophy (See p. 3, first paragraph). It is noted that the effective filing date of the Miller reference, with respect to PDT in combination with an anti-angiogenic agent is 2/10/2000.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wheeler and Miller to create the claimed method with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Miller who teaches using an antiangiogenic compound in combination with PDT.

8. Claims 16, 18-22 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over by U.S. Patent No. 6,248,741 (Wheeler et al.) as applied to claims 16, 18-22 above, and further in view of U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.; previously of record).

The '741 patent teaches a method of using brimonidine in combination with PDT, as indicated above.

The '741 patent does not teach that the method also comprises a therapeutically effective amount of an antiangiogenic compound.

However, Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound (e.g., see abstract; paragraph 18;

claims 20-31, etc.). It is noted that the instant specification acknowledges it was previously known that PDT can result in optic nerve atrophy (See p. 3, first paragraph). It is noted that the effective filing date of the Miller reference, with respect to PDT in combination with an anti-angiogenic agent is 2/10/2000.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wheeler and Miller to create the claimed method with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Miller who teaches using an antiangiogenic compound in combination with PDT.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 16, 18-22, 30, 39 and 40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,194,415 in view of Wheeler et al. (Euro. J. Opthalm, 1999; previously of record), and further in view of U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.; previously of record).

The claims of '415 are drawn to a method of protecting the optic nerve and retina of a mammal comprising administering to the mammal suffering from or at risk of suffering a noxious action on the nerve cells an effective amount of a compound of formula I to inhibit or prevent nerve cell injury or death, wherein the formula encompass brimonidine, and wherein the noxious action includes laser light directed into the eye in a procedure for treatment of wet ARMD. Claim 4 depends from claim 1 and recites that the noxious action is laser light directed into the eye in a procedure for treatment of wet ARMD.

The patent does not claim that the method comprises administering brimonidine as the compound of formula I or a therapeutically effective amount of an antiangiogenic compound.

However, Wheeler et al (1999) teaches brimonidine as a neuroprotective agent. Intraperitoneal brimonidine enhanced rat retinal ganglion cell survival and function in the partial crush injury model, and shown that the neuroprotection was dose-dependent. Topical application of brimonidine 1 hour before injury was effective in decreasing ischemic retinal injury. Ischemic retinas treated with brimonidine resulted with a large decrease in TUNEL staining. See the abstract on page S17, METHODS on pages S18-S19 and RESULTS and DISCUSSION on pages S20-S21.

Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound (e.g., see abstract; paragraph 18; claims 20-31, etc.). It is noted that the instant specification acknowledges it was previously known that PDT can result in optic nerve atrophy (See p. 3, first paragraph). It is noted that the effective filing date of the Miller reference, with respect to PDT in combination with an anti-angiogenic agent is 2/10/2000.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the indicated teachings to create the claimed method with a reasonable expectation of success.

11. Claims 16, 18-22, 39, 30 and 40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,248,741 in view of Wheeler et al. (Euro. J. Opthalm, 1999; previously of record) and further in view of U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.; previously of record).

The claims 1 of '741 is drawn to a method of protecting the optic nerve and retina of a mammal comprising administering to the mammal suffering from or at risk of suffering a noxious action on the nerve cells an effective amount of a compound of formula I to inhibit or prevent nerve cell injury or death, wherein the formula encompass brimonidine, and wherein the noxious action includes laser light directed into the eye in a procedure for treatment of wet

ARMD. Claim 7 depends from claim 1 and recites that the noxious action is laser light directed into the eye in a procedure for treatment of wet ARMD.

The patent does not claim that the method comprises administering brimonidine as the compound of formula I or a therapeutically effective amount of an antiangiogenic compound.

Wheeler et al (1999) teaches brimonidine as a neuroprotective agent. Intraperitoneal brimonidine enhanced rat retinal ganglion cell survival and function in the partial crush injury model, and shown that the neuroprotection was dose-dependent. Topical application of brimonidine 1 hour before injury was effective in decreasing ischemic retinal injury. Ischemic retinas treated with brimonidine resulted with a large decrease in TUNEL staining. See the abstract on page S17, METHODS on pages S18-S19 and RESULTS and DISCUSSION on pages S20-S21.

Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound (e.g., see abstract; paragraph 18; claims 20-31, etc.). It is noted that the instant specification acknowledges it was previously known that PDT can result in optic nerve atrophy (See p. 3, first paragraph). It is noted that the effective filing date of the Miller reference, with respect to PDT in combination with an anti-angiogenic agent is 2/10/2000.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings to create the claimed method with a reasonable expectation of success.

12. Claims 16, 18-22, 30, 39 and 40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,465,464 in view of Wheeler et al. (Euro. J. Opthalm, 1999; previously of record) and further in view of U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.; previously of record).

As indicated above, Wheeler et al. discloses and claims a method of providing neural protection including glaucomatous optic neuropathy to a mammal comprising administering to the mammal suffering from or at risk of suffering a noxious action on its nerve cells an effective amount of brimonidine to inhibit or prevent nerve cell injury or death (claim 1, column 17); wherein the noxious action is a laser light directed into the eye in a procedure for treatment of wet age-related macular degeneration (ARMD) (claim 7, column 18); administering an amount sufficient to achieve a serum concentration of from 0.01 nM to 500 nM (claim 15, column 18) or the compound is administered topically (claim 16, column 18). See also, claim 5.

The patent does not claim that the method comprises administering brimonidine as the compound of formula I or a therapeutically effective amount of an antiangiogenic compound.

Wheeler et al (1999) teaches brimonidine as a neuroprotective agent. Intraperitoneal brimonidine enhanced rat retinal ganglion cell survival and function in the partial crush injury

model, and shown that the neuroprotection was dose-dependent. Topical application of brimonidine 1 hour before injury was effective in decreasing ischemic retinal injury. Ischemic retinas treated with brimonidine resulted with a large decrease in TUNEL staining. See the abstract on page S17, METHODS on pages S18-S19 and RESULTS and DISCUSSION on pages S20-S21.

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Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings to create the claimed method with a reasonable expectation of success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner
Art Unit 1635